# THE EFFECT OF INTERMITTENT EXPOSURE TO 3% $CO_2$ ON RESPIRATION

by

K. E. Schaefer,
C. R. Carey,
and
J. H. Dougherty, Jr.

SUBMARINE MEDICAL RESEARCH LABORATORY
NAVAL SUBMARINE MEDICAL CENTER REPORT NO. 618

Bureau of Medicine and Surgery, Navy Department
Research Work Unit M4306.02-7050B.01

Reviewed and Approved by:

Charles F. Gell

Charles F. Gell, M.D., D.Sc. (Med)
Scientific Director
SubMedResLab

Reviewed and Approved by:

Joseph D Bloom.

J. D. Bloom, CDR MC USN
Director
SubMedResLab

Approved and Released by:

J E Stark

J. E. Stark, CAPT MC USN
COMMANDING OFFICER
Naval Submarine Medical Center

## SUMMARY PAGE

### THE PROBLEM

To determine whether intermittent exposure to 3% $CO_2$ results in a saturation of the body with carbon dioxide and whether a compensation of the respiratory acidosis induced by carbon dioxide inhalation occurs.

### FINDINGS

Intermittent exposure of one subject for six days to increased $CO_2$ for fifteen hours produced a transient filling and emptying of $CO_2$ stores within a five-day period, leading to normal alveolar $CO_2$ levels and gas exchange data on the sixth day. An equilibrium was obtained after five days at a normal alveolar and blood $CO_2$ level in contrast to continuous exposure to 3% $CO_2$, in which an equilibrium is obtained at an elevated blood and tissue $CO_2$ level. It is concluded therefore that intermittent exposure to 3% $CO_2$ does not lead to a prevailing saturation of the organism with $CO_2$ or a compensation of the respiratory acidosis. The ventilatory response to $CO_2$ is increased during intermittent exposure to $CO_2$, rather than decreased as is the case in chronic hypercapnia (3% $CO_2$).

### APPLICATIONS

These findings are of importance for submarine medical officers dealing with carbon dioxide toxicity in submarines, and for scientists interested in the effects of carbon dioxide.

## ADMINISTRATIVE INFORMATION

This investigation was conducted as a part of Bureau of Medicine and Surgery Research Work Unit M4306.02-7050B - Physiological Effects of Intermittent Exposure to Increased $CO_2$ and Lowered $O_2$ Levels. The present report is No. 1 on this Work Unit. The manuscript was approved for publication on 20 March 1970 and designated as Submarine Medical Research Laboratory Report No. 618.

PUBLISHED BY THE NAVAL SUBMARINE MEDICAL CENTER

# ABSTRACT

An investigation was conducted to determine whether intermittent exposure to 3% $CO_2$ results in a saturation of the body with carbon dioxide and whether a compensation of the respiratory acidosis is induced by carbon dioxide inhalation.

One healthy male subject was exposed for six days, 15 hours daily, to a $CO_2$ concentration rising from 0 - 3% at normal oxygen concentrations of 20 - 21% $O_2$.

Average data of physiological measurements made (A) prior to and (B) at the end of the 15-hour exposure to $CO_2$ concentration, rising linearly from 0 - 3% $CO_2$ were $PA_{CO_2}$ (A); 40.7 mm Hg; $P_{A_{CO_2}}$ (B): 42 mm Hg; $P_{A_{O_2}}$ (A): 100.7 mm Hg; $P_{A_{O_2}}$ (B): 114.8 mm Hg; $V_E$(A): 6.28 L/m; $V_E$ (B): 12.09 L/m.

$P_{A_{CO_2}}$ determined at the end of the nine-hour air breathing rose from the third day on to reach, at the fifth day, a peak higher than the corresponding value following 15 hours of $CO_2$ inhalation. During the sixth day of intermittent exposure to $CO_2$, $P_{A_{CO_2}}$ on air returned to control values. This finding indicates that after three days the nine-hour period of air breathing was insufficient to eliminate the $CO_2$ accumulated during the 15-hour period of $CO_2$ breathing.

Ventilatory response to 5% $CO_2$ was increased during intermittent exposure to $CO_2$ and the slope of the $CO_2$ tolerance curve was also increased.

THE EFFECT OF INTERMITTENT EXPOSURE TO 3% $CO_2$ ON RESPIRATION

## INTRODUCTION

Compensation of the respiratory acidosis produced by inhalation of moderate $CO_2$ concentration (3% $CO_2$ = 21 mm Hg) has been found to require approximately five days in man[2,3,4]. During this adaptation to $CO_2$, a reduction in the ventilatory response occurs. Studies on intermittent exposure to 3% $CO_2$ have not been reported. The purpose of this investigation was to determine whether a compensation of the respiratory acidosis is reached during intermittent exposure to 3% $CO_2$.

## METHODS

Resting respiratory minute volume ($\dot{V}_E$), oxygen consumption ($\dot{V}_{O_2}$) carbon dioxide excretion ($\dot{V}_{CO_2}$), alveolar carbon dioxide and oxygen tensions ($P_{A_{CO_2}}$) and ($P_{A_{O_2}}$) were measured twice daily, between 8-9 AM and 10:30-11:00 PM. Average end tidal gas samples were collected with a Rahn sampler and analyzed with a Beckman LB-1 infrared $CO_2$ meter and a Servomex $O_2$ meter. Mixed expired gas was collected in a Douglas bag for the last six minutes of the ten-minute test period. Volume measurements were made with a dry gas meter.

The respiratory rate was determined with a Yellow Springs thermistor inserted at the side of the mouthpiece.

$CO_2$ tolerance tests consisting of ten-minute inhalation of 5% $CO_2$ in 21% $O_2$ were carried out on six occasions, twice daily following the measurement of resting ventilation.

## RESULTS

The effect of intermittent exposure to $CO_2$ on pulmonary ventilation and alveolar gas tensions is shown in Figure 1 and Table I. Respiratory minute volume increased to twice the resting ventilation on air at the end of the 15-hour exposure to rising $CO_2$ concentration reaching 3% $CO_2$ at the time the measurement was made. Alveolar $CO_2$ tension rose from 40.7 mm Hg to 42.4 mm Hg while the alveolar $O_2$ tension increased from 100.7 mm Hg to 114.8 mm Hg. All the values obtained after nine hours of air breathing remained at control levels with the exception of the alveolar $CO_2$ tension, which rose on the fourth and fifth day, reaching a peak which was

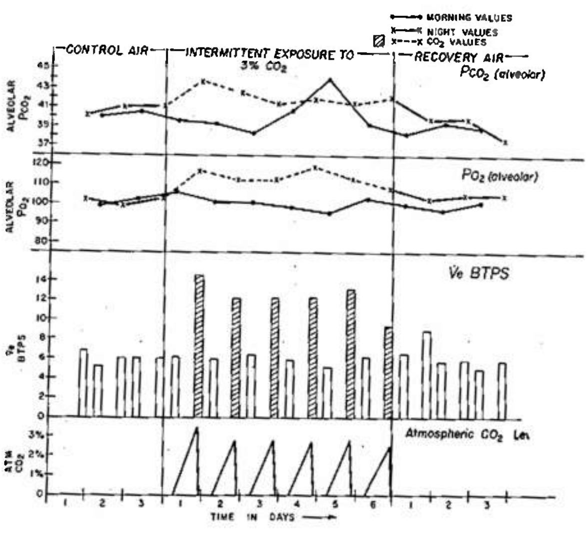


Figure 1

Table I. Effect of Intermittent Exposure to 3% $CO_2$ on Respiratory Minute Volume ($\dot{V}e$), Alveolar Carbon Dioxide ($P_{A_{CO_2}}$) and Oxygen Tension ($P_{A_{O_2}}$)

| Condition | | $\dot{V}_E$ BTPS L/min | $P_{A_{CO_2}}$ mm Hg | $P_{A_{O_2}}$ mm Hg |
|---|---|---|---|---|
| Control 8 AM | Mean | 5.68 | 40.7 | 101.0 |
| | N | 2 | 2 | 2 |
| Control 11 PM | Mean | 6.22 | 42.4 | 100.7 |
| | SEM | .27 | 1.2 | 1.2 |
| | N | 3 | 3 | 3 |
| Experi-mental 9 hours on air | Mean | 5.99 | 40.4 | 101.8 |
| | SEM | .17 | .9 | 1.4 |
| | N | 6 | 6 | 6 |
| Exposure 15 hours on $CO_2$ (0-3% $CO_2$) 11 PM | Mean | 12.35 * ** | 42.4 | 114.8 * ** |
| | SEM | .70 | .4 | 1.5 |
| | N | 6 | 6 | 6 |
| Recovery on air 8 AM | Mean | 5.79 | 39.0 | 100.8 |
| | SEM | .47 | .2 | 1.2 |
| | N | 3 | 3 | 3 |
| Recovery on air 11 PM | Mean | 6.59 | 38.8 | 105.0 |
| | SEM | .70 | 1.4 | .7 |
| | N | 3 | 3 | 3 |

* Statistically different from control levels.

** Statistically significant difference between data obtained after 9 hours on air (8AM) and 15 hours on $CO_2$ (0-3% $CO_2$) at 11 PM even higher than the corresponding value on $CO_2$ breathing. This indicates that the nine-hour period of air breathing was, after three days, not sufficient to eliminate the previously accumulated $CO_2$.

Data on oxygen consumption, $CO_2$ excretion and respiratory exchange ratio are presented in Table II and daily changes in Figure 2. $CO_2$ excretion is consistently elevated during $CO_2$ breathing while the oxygen consumption does not change significantly. It should be noted that the oxygen consumption during air breathing tends to decline, a condition which leads to an increase of the respiratory exchange ratio during the fourth and fifth day corresponding to the rise in alveolar $CO_2$ tension. The subsequent return of the respiratory exchange ratio to near normal values on the sixth day of intermittent $CO_2$ exposure, which is paralleled by the fall in alveolar $CO_2$ tension, suggests that the more rapidly exchanging $CO_2$ stores of the body were able to give up the previously accumulated $CO_2$ during two air breathing periods of 18 hours.

The ventilatory response to inhalation of 5% $CO_2$ increased during the sixth day of intermittent exposure to 3% $CO_2$, as shown in Table III. $P_{A_{CO_2}}$ tended to decrease and $P_{A_{O_2}}$ to rise. The slope of $CO_2$ tolerance curves increased during the intermittent exposure to $CO_2$ and during the recovery period on air.

Intermittent exposure to 3% $CO_2$ had effects on lung functions (Table IV). Vital capacity was found decreased at the end of the 15-hour period of $CO_2$ exposure and also in the morning after a 9-hour period of air breathing. The same is true for the expiratory reserve volume, while inspiratory capacity was unaffected. The maximum expiratory flow rates (MEFR) did decrease, not only during the experimental period, but remained below control levels during the recovery period on air, in contrast to the maximal inspiratory flow rates (MIFR) which did not change.

## DISCUSSION

The experimental design in this study of intermittent exposure to $CO_2$ required the scheduling of measurements at 8 AM, prior to eating, and 11 PM, three hours after supper. Diurnal variations of physiological functions therefore influence the measurements and comparisons have to be made of corresponding time periods.

Moreover, the alternating periods of air breathing and $CO_2$ breathing during intermittent exposure exhibit both $CO_2$ effects. In the former, $CO_2$ accumulates during the fourth and fifth day while the latter shows a direct effect of $CO_2$ inhalation.

In the recovery period on air, alveolar and blood carbon dioxide quickly return to control values after eight hours of air breathing and remain at this level but the main carbon dioxide elimination occurs on the second day of recovery, as indicated in a large excretion of urine bicarbonate[6]. This suggests that metabolic effects of $CO_2$ are still present at a

Table II. Effect of Intermittent Exposure to 3% $CO_2$ on Carbon Dioxide Excretion ($\dot{V}_{CO_2}$), Oxygen Consumption ($\dot{V}_{O_2}$) and Respiratory Exchange Ratio (R)

| Condition | | $\dot{V}_{CO_2}$ | $\dot{V}_{O_2}$ | R |
|---|---|---|---|---|
| Control 8 AM | Mean | 186.5 | 236.0 | .79 |
| | N | 2 | 2 | 2 |
| Control 11 PM | Mean | 205.7 | 252.7 | .81 |
| | SEM | 6.2 | 8.2 | .01 |
| | N | 3 | 3 | 3 |
| Experi-mental 9 Hours on air 8 AM | Mean | 189.2 | 223.8 | .86 |
| | SEM | 3.0 | 10.9 | .04 |
| | N | 6 | 6 | 6 |
| Exposure 15 hours on $CO_2$ (0-3% $CO_2$) 11 PM | Mean | 228.2 ** | 248.5 | .92 * |
| | SEM | 7.8 | 11.1 | .02 |
| | N | 6 | 6 | 6 |
| Recovery on air 8 AM | Mean | 183.3 | 236.3 | .78 |
| | SEM | 12.0 | 12.2 | .02 |
| | N | 3 | 3 | 3 |

* Statistically significantly different from control levels at the 5% level.

** Statistically significant difference between data obtained after 9 hours on air (8 AM) and 15 hours on $CO_2$ (0-3% $CO_2$) at 11 PM at the 5% level and better

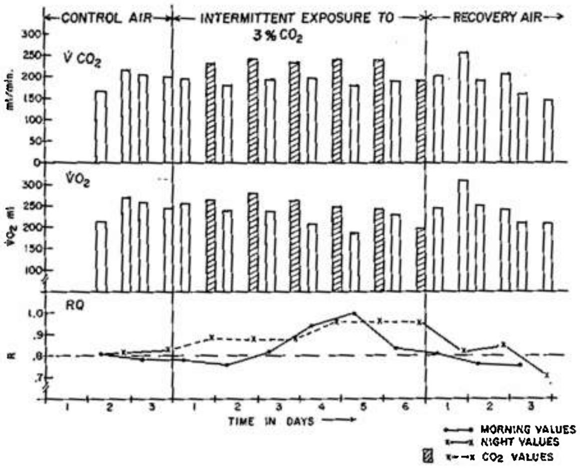


Figure 2

time of the recovery period when alveolar and blood $CO_2$ tensions are essentially normal.

The preliminary study on intermittent exposure to 3% $CO_2$ produced two essential findings which are in contrast to the well known effects of chronic exposure to 3% $CO_2$:

1. A transient filling and emptying of $CO_2$ stores of the body within a five-day period resulting in normal alveolar $CO_2$ tensions and pulmonary gas exchange data on the day of intermittent exposure. This indicates that pulmonary and renal regulations[6] stimulated by accumulated $CO_2$, are adequate to attain an equilibrium at a normal $CO_2$ level rather than at an elevated $CO_2$ level, as in chronic hypercapnia. One can, therefore, not speak about a compensation of a respiratory acidosis.

It is interesting to note one similarity between intermittent and chronic

Table III. Effect of Intermittent Exposure to $CO_2$ For Six Days on Ventilatory Response to 5% $CO_2$, Alveolar Gas Tension and Slope of $CO_2$ Tolerance Curves

| Conditions | | $\dot{V}_E$ L/m BTPS | $P_{A_{CO_2}}$ mm Hg | $P_{A_{O_2}}$ mm Hg | Slope of $CO_2$ tolerance curves |
|---|---|---|---|---|---|
| Control | Mean | 19.58 | 49.5 | 132.7 | .365 |
| | Range | (18.9-20.3) | (49.0-50.0) | (131.7-133.7) | (.31-.42) |
| | N | 2 | 2 | 2 | 2 |
| Intermittent $CO_2$ period of 6 days | Mean | 24.37 | 47.04 | 136.7 | .493 |
| | S. E. | (1.64) | (0.59) | (.75) | (.031) |
| | N | 6 | 6 | 6 | 6 |
| Recovery on air | Mean | 21.62 | 45.06 | 135.1 | .520 |
| | S. F. | (.80) | (.33) | (1.77) | (.042) |
| | N | 4 | 4 | 4 | 4 |

Table IV. Effect of Intermittent Exposure to 3% $CO_2$ on Lung Functions, Vital Capacity (VC), Inspiratory Capacity (IC), Expiratory Reserve Volume (ERV), Maximum Expiratory Flow Rate (MEFR), Maximum Inspiratory Flow Rate (MIFR), Maximum Voluntary Ventilation (MVV)

| Condition | | VC liters | IC liters | ERV liters | MEFR L/sec | MIFR L/sec | MVV L/min |
|---|---|---|---|---|---|---|---|
| Control 8 AM | Mean | 5.83 | 3.61 | 2.22 | 14.05 | 12.66 | 198 |
| | SEM | .08 | .01 | .08 | .15 | .28 | 16 |
| | N | 3 | 3 | 3 | 3 | 3 | 3 |
| Control 11 PM | Mean | 5.87 | 3.95 | 1.93 | 13.51 | 12.18 | 210 |
| | SEM | .07 | .10 | .03 | .34 | .54 | 12 |
| | N | 3 | 3 | 3 | 3 | 3 | 3 |
| Experi-mental on air 8 AM | Mean | 5.62 | 3.68 | 1.94* | 12.90* | 12.74 | 225 |
| | SEM | .05 | .04 | .04 | .27 | .15 | 3 |
| | N | 6 | 6 | 6 | 6 | 6 | 6 |
| Experi-mental on 3% $CO_2$ 11 PM | Mean | 5.73 | 3.97 | 1.77 | 12.94 | 12.82 | 225 |
| | SEM | .03 | .07 | .07 | .16 | .20 | 5 |
| | N | 6 | 6 | 6 | 6 | 6 | 6 |
| Recovery 8 AM | Mean | 5.67 | 3.91* | 1.76* | 12.56* | 12.55 | 244 |
| | SEM | .06 | .07 | .01 | .11 | .27 | 3 |
| | N | 3 | 3 | 3 | 3 | 3 | 3 |
| Recovery 11 PM | Mean | 5.80 | 3.97 | 1.82 | 12.45 | 12.96* | 245* |
| | SEM | .01 | .14 | .01 | .48 | .23 | 2 |
| | N | 3 | 3 | 3 | 3 | 3 | 3 |

* Statistically significant difference from control levels at the 5% confidence level.

exposure to 3% $CO_2$. The same time period of five days is required to come back to control levels in the first case and reach a compensation of the respiratory acidosis in the second case.

2. Findings of an increased ventilatory response to $CO_2$ and increased slope of the $CO_2$ response curve during intermittent exposure to 3% $CO_2$ are opposite to the depression of ventilatory response and decrease in slope observed in chronic exposure to 3% $CO_2$[3].

The decrease in vital capacity observed during the experimental period, both during air breathing and during $CO_2$ breathing, is associated with a decrease in expiratory reserve volume which might be caused by blood volume shifts into the thorax, due to $CO_2$ inhalation or the slow accumulation of $CO_2$ during the air breathing period.

The decrease in MEFR of approximately one liter/second, observed during both experimental periods and during the third day of recovery period, suggests a $CO_2$ induced increase in airway resistance.

Hypercapnia induced by inhalation of 7% $CO_2$ has been found to increase airway resistance[7] but ten minute exposure to lower $CO_2$ concentrations (4-10%) did not change airway resistance[1]. Our findings seem to suggest that prolonged exposure of 15 hours to a $CO_2$ concentration rising to 3% $CO_2$ has an effect on airway resistance. More investigations on a larger group of subjects are needed to clarify this effect of $CO_2$.

## REFERENCES


1. Butler, J., Caro, C.G., Alcala, R. and DuBois, A.B. Physiological factors affecting airway resistance in normal subjects and in patients with obstructive disease. J. Clin. Invest. 39:584-591, 1960.

2. Chapin, J.L., Otis, A.B., and Rahn, H. Changes in the sensity of the respiratory center in man after prolonged exposure to 3% $CO_2$. Wright Air Dev. Cen. Tech. Report 55-357, pp. 250-254, 1956.

3. Clark, T.M., Sinclair, R.D., and Welch, E.B. Rate of acclimatization to chronic hypercapnia in man. In: Proc. 4th Symp. on Underwater Physiol. Ed. C.J. Lambertsen, Philadelphia, 1970.

4. Schaefer, K.E. Respiratory and acid base balance during prolonged exposure to a 3% $CO_2$ atmosphere. Pflüger's Arch. ges. Physiol. 251:689-715, 1949.

5. Schaefer, K.E. A concept of triple tolerance limits based on chronic carbon dioxide toxicity studies. Aerospace Med. 32:197-204, 1961.

6. Schaefer, K.E., A. Messier, and C. Morgan. Effect of intermittent exposure to 3% $CO_2$ on acid base balance. Sub. Med. Res. Lab., Sub. Med. Cen. report in preparation

7. Sterling, G.M. The mechanism of decreased specific airway conductance in man during hypercapnia caused by inhalation of 7% $CO_2$. Clin. Science. 37:539-548, 1969.

UNCLASSIFIED
Security Classification

# DOCUMENT CONTROL DATA - R & D

*(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)*

| | |
|---|---|
| 1. ORIGINATING ACTIVITY *(Corporate author)*<br>NAVAL SUBMARINE MEDICAL CENTER<br>Submarine Medical Research Laboratory | 2a. REPORT SECURITY CLASSIFICATION<br>UNCLASSIFIED<br>2b. GROUP |

3. REPORT TITLE
THE EFFECT OF INTERMITTENT EXPOSURE TO 3% $CO_2$ ON RESPIRATION

4. DESCRIPTIVE NOTES *(Type of report and inclusive dates)*
Interim Report

5. AUTHOR(S) *(First name, middle initial, last name)*
K. E. Schaefer, C. R. Carey, and J. H. Dougherty, Jr.

| 6. REPORT DATE | 7a. TOTAL NO. OF PAGES | 7b. NO. OF REFS |
|---|---|---|
| 13 March 1970 | 7 | 7 |

| | |
|---|---|
| 8a. CONTRACT OR GRANT NO. | 9a. ORIGINATOR'S REPORT NUMBER(S) |
| b. PROJECT NO. M4306.02-7050B | SMRL Report Number 618 |
| c. | 9b. OTHER REPORT NO(S) *(Any other numbers that may be assigned this report)* |
| d. | |

10. DISTRIBUTION STATEMENT
This document has been approved for public release and sale; its distribution is unlimited.

| 11. SUPPLEMENTARY NOTES | 12. SPONSORING MILITARY ACTIVITY |
|---|---|
| | Naval Submarine Medical Center<br>Box 600 Naval Submarine Base<br>Groton, CT 06340 |

13. ABSTRACT


One healthy male subject was exposed for six days, 15 hours daily, to a $CO_2$ concentration rising from 0 - 3% $CO_2$ at normal oxygen concentrations of 20 - 21% $O_2$

Average data of physiological measurements made (A) prior to and (B) at the end of the 15-hour exposure to $CO_2$ concentration, rising linearly from 0 - 3% $CO_2$ were $P_{ACO_2}$(A): 40.7 mm Hg; $P_{ACO_2}$(B): 42 mm Hg; $P_{AO_2}$(A): 100.7 mm Hg; $P_{AO_2}$(B): 114.8 mm Hg; $\dot{V}_E$(A): 6.28 L/m; $\dot{V}_E$(B): 12.09 L/m.

$P_{ACO_2}$ determined at the end of the nine-hour air breathing rose from the third day on to reach, at the fifth day, a peak higher than the corresponding value following 15 hours of $CO_2$ inhalation. During the sixth day of intermittent exposure to $CO_2$, $P_{AO_2}$ on air returned to control values. This finding indicates that after three days the nine-hour period of air breathing was insufficient to eliminate the $CO_2$ accumulated during the 15-hour period of $CO_2$ breathing.

Ventilatory response to 5% $CO_2$ was increased during intermittent exposure to $CO_2$ and the slope of the $CO_2$ tolerance curve was also increased.


DD FORM 1473 1 NOV 65 (PAGE 1)

S/N 0101-807-6801

UNCLASSIFIED
Security Classification

3ND PPSO 13152

| 14. KEY WORDS | LINK A | | LINK B | | LINK C | |
|---|---|---|---|---|---|---|
| | ROLE | WT | ROLE | WT | ROLE | WT |
| Intermittent exposure to $CO_2$ | | | | | | |
| Carbon dioxide toxicity | | | | | | |
| Respiration | | | | | | |
| $CO_2$ Sensitivity | | | | | | |